Effect of Cocaine-Related Environmental Stimuli on the Spontaneous Electroencephalogram in Polydrug Abusers

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Relationships between the spontaneous electroencephalogram (EEG), self-reports of cocaine craving, and cerebral glucose metabolism, determined using 2-[^{18}F]fluoro-2-deoxy-D-glucose and positron emission tomography, were assessed during the presentation of either neutral or cocaine-related environmental stimuli. In cocaine users but not non-drug-abusing controls, EEG power in the alpha$_1$ and alpha$_2$ frequency bands was significantly lowered during presentation of the drug-related stimuli when compared with the neutral test session. Decreases in

*alpha$_1$ power were negatively correlated with increases in global glucose metabolism but were not correlated with either the time course or the magnitude of craving throughout the 30-min test session. Although EEG desynchronization is related to global brain metabolism, the difference in the time courses between EEG power and craving suggests that self-reports of cue-elicited cocaine craving do not simply reflect increases in the state of cortical arousal.   [**Neuropsychopharmacology 19:10–17, 1998**]. Published by Elsevier Science Inc.*

Exposure to drug-related stimuli in a laboratory setting or in a natural environment can elicit behavioral and physiological arousal and drug craving in individuals with addictive disorders (Avants et al. 1993; Bauer and Kranzler 1994). This cue-elicited craving coupled with reports from addicts themselves attributing relapse to episodes of drug craving, although the proportion of substance abusers reporting an association of craving with relapse exhibits notable variability among study populations (Wikler, 1948; Childress et al. 1992; Drummond et al. 1995), has created substantial interest in the

neurophysiological mechanisms by which relevant stimuli evoke such craving (Stewart et al. 1984; Wise 1987; Siegel 1991; Childress et al. 1992; Avants et al. 1993; Robinson and Berridge 1993).

Published data on the cerebral substrates of cue-elicited cocaine craving in humans have been limited to reports that drug-related cues produce diffuse decreases in the power of the electroencephalogram (EEG) (Bauer and Kranzler 1994) and induce activation of cortical and limbic areas of brain indexed by rates of regional cerebral glucose metabolism (Grant et al. 1996). Changes in glucose metabolism in the dorsolateral prefrontal cortex, amygdala, and cerebellum were correlated with the change in craving from a neutral session to one in which cocaine-related cues were presented (Grant et al. 1996). Because the cerebral metabolic rate for glucose determined by positron emission tomography (PET) is a single measurement representing a time-weighted integration of brain activity over a 30-min period, it was not possible to directly compare changes in brain glucose metabolism to the time course of craving, which was measured at three times during the 30 min. There-

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fore, the spontaneous EEG also was recorded during the presentation of neutral cues and drug-related cues. The objective of the present work was to examine the time-dependent changes in the components of the EEG spectrum between the neutral cues and cocaine cues sessions and the relation of such changes in EEG activity to changes in subjective self-reports of cocaine craving and the global cerebral metabolic rate for glucose (CMRglc).

Based upon previous work (Bauer and Kranzler 1994), it was expected that drug-related stimuli would produce EEG signs of arousal (i.e., decreases in EEG power) that would be more robust than those measured during presentation of non-drug cues to experienced cocaine users. Because the duration of the cues session in the present study was much longer (30 min) than in the study by Bauer and Kranzler (5 min), it was also possible to characterize the time course of changes in the EEG spectrum and test whether changes in EEG spectral power were temporally related to subjective self-reports of cocaine craving. Finally, the relation of changes in global cerebral glucose metabolism to changes in EEG activation across sessions was examined.

METHODS

Subjects

A total of 17 male cocaine abusers, ranging in age from 25 to 40 years (mean 32 years), and five control subjects (4 men, 1 woman), who were 24 to 29 years of age (mean 27 years), were recruited to study the effects of drug-related environmental cues on cerebral glucose utilization measured by PET and the spontaneous EEG. Of the 17 cocaine abusers, simultaneous EEG and PET data were obtained from eight subjects. All subjects received a physical examination before giving informed consent for participation in the study. Evidence of physical disease, a history of head trauma with loss of consciousness, or fulfillment of criteria for any Axis I psychiatric disorder, other than substance abuse or dependence, or for any Axis II disorder, other than borderline or antisocial personality disorder, were exclusionary criteria (for details, see Grant et al. 1996). All subjects in the cocaine-using group reported long-term use of cocaine as well as other illicit substances. Their cocaine intake history was characterized by 8.8 years of use (median 8 years; range 2.5 to 20 years) with a current mean use of 1.9 g/week (median 1.75, range 0.2 to 4.3 g/week). The incidence of other current substance abuse was as follows: heroin (8/17 subjects), marijuana (14/17), alcohol (17/17), and nicotine (15/17). None of the subjects was physically dependent on opiates or alcohol, nor were any receiving treatment for drug abuse. Within the control group, none reported cocaine, heroin, or marijuana use, two of five subjects smoked cigarettes, and all five used alcohol. Fourteen of the subjects in the cocaine group were right-handed, one was left-handed, and two were ambidextrous; three of the control subjects were right-handed, and two were left-handed according to responses on a questionnaire (Annett 1970).

General Procedures

Subjects participated in two test sessions separated by at least 1 week as described previously (Grant et al. 1996). The procedures were approved by the Institutional Review Boards of National Institute on Drug Abuse (NIDA) and the Johns Hopkins Bayview Medical Center, where the Intramural Research Program of NIDA is located. To avoid the acute effects of alcohol or illicit drugs of abuse from confounding the test results, all subjects in the cocaine abuser group resided on a closed ward at the Addiction Research Center (ARC), NIDA for at least 2 days before each test session; control subjects were domiciled on the night before each session in a separate facility within the ARC. Subjects, however, did not remain in the ARC during the time between the two sessions. Control subjects left the ARC immediately after the conclusion of the PET session; however, drug abusers were required to remain on the ARC ward overnight and were discharged the next day. Cocaine use was verified by urinalysis upon admission to the ward prior to each session.

On study days, subjects were prepared with arterial and venous catheters, which were required for the PET component of the study, and EEG leads were placed before the subjects were moved to a soundproof isolation chamber. Throughout the experiment, subjects were seated in a reclining chair, and pink noise (75 dB) was presented through speakers in the room and via headphones to mask extraneous sounds. The experimental sequence consisted of measurement of baseline values for the EEG, other physiological measures, and subjective reports; injection of the radiotracer, 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG) intravenously over 15 s or a simulated injection, and a 30-min presentation of either a neutral or cocaine-related stimulus complex, while the EEG data, physiological measures, and self-reports of cocaine craving were collected in 10-min epochs. Subjects were instructed to keep their eyes focused on the stimulus complex and to refrain from unnecessary talking and movement (including eye blinks) except when providing subjective self-reports. These reports were obtained immediately before presentation of the stimulus complex and at 10, 20, and 30 min after FDG injection or simulated injection. The self-report instrument consisted of five questions: "How good do you feel?", "Do you have a craving or urge for cocaine?", "Do you want cocaine?", "Do you need cocaine?", and "Are you turned off?". The subjects responded verbally on a scale

of 0 to 10, with "0" indicating "not at all" and "10" indicating "extremely."

The neutral and cocaine-related stimulus complexes each consisted of a videotape and objects related to either arts and crafts (leather punch and paint brush) or cocaine use (glass pipe, mirror, razor blade, straw, a $10 bill, and 48 mg of l-cocaine HCl from the Research Technology Branch, NIDA), respectively. To increase the likelihood of eliciting craving in the cocaine abuser group, subjects in that group were told that they would be allowed to self-administer (by insufflation) the cocaine in view after completion of the experimental procedures (including acquisition of brain scans). To preclude the possibility of drug-related associations with the experimental environment, the neutral stimulus complex was always presented during the first session, and the cocaine-related stimulus complex was presented during the second session.

EEG Recording

An electrode cap with 22 Ag/AgCl electrodes was used for EEG acquisition (Electro-Cap, Eaton, OH). There were 19 cortical leads (F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fpz, Fz, Cz, Pz, and Oz) configured according to the International 10-20 System (Jasper 1958). During recording, all leads were referenced to the tip of the nose. Interelectrode impedances were maintained below 5 kΩ. The electric signals were amplified (gain = 20,000) and filtered (bandpass = 0.1 to 50 Hz) by a Grass Model 12 Neurodata Acquisition System. Vertical and horizontal eye movement (EOG) activity, muscle activity (EMG) produced by smiling (zygomatic muscle) and frowning (corrugator muscle), and a 3-lead electrocardiogram (ECG) were recorded on separate channels. All channels of EEG, EMG, and ECG activity were digitized at a rate of 256 samples/s/channel using a PC-based data acquisition system (EEGSYS, v 5.5, Friends Medical Science Research Center, Inc., Baltimore, MD), monitored "on-line," and saved for later "off-line" analysis. Physiological activity was monitored and acquired across four periods in each session, starting with a 7-min eyes open baseline period followed by three 10-min blocks during the 30-min stimulus complex presentation. For the last 12 of the 17 subjects, an eyes-closed (5-min) baseline recording was collected before the eyes-open baseline.

Only data from the electrodes in the central and parietal areas (C3, C4, P3, P4, Cz, and Pz) were analyzed due to the high incidence of artifacts in the temporal, frontal, and occipital electrode recordings. Before initiating spectral analysis, EEG data were re-referenced to the linkage of the two ear lobe electrodes and edited to select artifact-free epochs. Each epoch contained 2 s of contiguous EEG data, and the interval between epochs varied. Data editing started at the first data point of

each acquisition period until a maximum of 60 such epochs had been selected for a total of 2 min. Some periods had less than 60 artifact-free epochs available, but the minimum number of epochs for a period was 40 (1 min, 20 s). A *cosine* taper-transformation was placed at the beginning and end of each epoch before the EEG data were converted to the frequency domain at a resolution of 0.5 Hz with a Fast Fourier Transformation. The resulting spectra were averaged over the epochs comprising each period. Frequency bands were defined as follows: delta (1 to 3.5 Hz), theta (4 to 7.5 Hz), alpha$_1$ (8 to 10.5 Hz), alpha$_2$ (11 to 13 Hz), beta$_1$ (13.5 to 17 Hz), beta$_2$ (17.5 to 30 Hz), and fast activity (30.5 to 50 Hz).

Cerebral Glucose Metabolism

CMRglc was measured by PET using FDG as the radiotracer, as described previously (Grant et al. 1996). Briefly, FDG was infused IV about 1 min after the visual stimulus complex was first presented and approximately 34 arterial blood samples were drawn over the course of the experiment. Plasma was assayed for radioactivity and glucose to provide input functions for an operational equation (Phelps et al. 1979; Reivich et al. 1979). CMRglc was taken as the area-weighted average metabolic rate for glucose in each of the 12 transaxial slices assayed.

Statistical Analysis

The absolute EEG power during each cue-present period relative to the baseline period was transformed into a percent change score (van Winsum et al. 1984; Pickworth et al. 1986; Sergeant et al. 1987; Knott et al. 1995). The distributions of the transformed scores were tested for normality using the Shapiro-Wilk W statistic and visual inspection of the distributions, as both raw EEG power measures and percentage transformations can be non-normally distributed (Gasser et al. 1982). No further transformation of the data was performed because (1) nearly all of the data were not significantly different from a normal distribution, (2) those few data that had non-normal distributions were not uniformly associated with an individual lead, time point or EEG power band, (3) standard transformations, e.g., arcsin or log transformations, do not greatly improve the normality of EEG data (Gasser et al. 1982), and (4) the ANOVA is robust against moderate departures from normality (Kirk 1982). The percent change data were analyzed using a 3-way repeated measures analysis of variance (ANOVA), with sessions, time (1 to 10, 11 to 20, and 21 to 30 min), and leads as repeated measures. Prior to calculating the change scores, potential differences in the absolute power for each EEG band between the two pre-cue, eyes-open baseline recording periods were evaluated with a 2-way repeated measures ANOVA,

with sessions (cocaine vs. neutral) and leads (C3, C4, P3, P4, Cz, and Pz) as the repeated measures factors. Because of the small n for the control group, which effectively decreased the power of analyses incorporating both groups, each of the subject groups was analyzed separately as well as collectively by adding a between-groups factor to form a mixed model ANOVA. Scores for each item of the self-reported craving scale were converted to change scores by subtracting the baseline score from the score obtained after each 10-min period of EEG acquisition. The change scores were then analyzed using a 2-way repeated measures ANOVA, incorporating sessions (cocaine vs. neutral) and time (1 to 10, 11 to 20, and 21 to 30 min) as repeated measure factors. Statistical analysis was performed using the SAS Program for Statistical Analysis® (Carey, NC). Statistical inferences were adjusted for deviations from homogeneity and sphericity assumptions with the Geisser-Greenhouse procedure as recommended for repeated measures ANOVA designs (Kirk 1982).

Pearson correlations were used to assess relationships between EEG power and self-reported craving, and between EEG power and CMRglc. Composite values for changes in alpha$_1$ and alpha$_2$ power were derived by averaging the changes in all six leads across all three 10-min observation periods within a test session. To determine the correlation of changes in EEG power with CMRglc, cumulative, 30-min EEG values were obtained by averaging the percent change in each of the six leads within each 10-min cue presentation period and summing the average percent changes from baseline over the three presentation periods. Differences in cumulative, 30-min EEG power (cocaine cues − neutral cues) were then tested for their correlation with corresponding differences in CMRglc.

RESULTS

EEG Data

Analysis of the combined eyes-open EEG baseline absolute power demonstrated no difference between the cocaine user and control groups (groups main effect) and no difference between sessions or session × group effects. There were significant leads effects and leads × group interactions for both alpha$_1$ [$F(5,100) = 5.88$, $p < .01$; $F(5,100) = 3.64$, $p < .05$] and alpha$_2$ [$F(5,100) = 5.70$, $p < .01$; $F(5,100) = 3.66$, $p < .05$] bandwidths, respectively, and a significant session × leads interaction [$F(5,100) = 3.26$, $p < .01$] for the theta frequency.

For the cocaine user group, the percentage change in absolute power in the alpha$_1$ and alpha$_2$ bands was differentially affected by the presentation of cocaine-related cues relative to the neutral cues. A significant main effect of session (neutral vs. cocaine) on the percentage of

change in EEG power was demonstrated for the alpha$_1$ [$F(1,16) = 6.66$, $P < .05$] and alpha$_2$ [$F(1,16) = 6.27$, $p < .05$] bands. EEG responses to cue presentations were characterized by greater reductions in alpha power during the cocaine cues session than during the neutral cues session (Figure 1). Power in the remaining bandwidths also tended to be lower throughout the cocaine cues session relative to the neutral cues session, but these differences were not statistically significant (Figure 2). However, total power determined for the cocaine cues session was significantly lower than that during presentation of the neutral cues [$F(1,16) = 7.92$, $p < .01$] (data not illustrated).

A significant main effect of time (sequential recording periods) was found across all EEG bands [delta: $F(2, 32) = 5.60$, $p < .01$; theta: $F(2, 32) = 27.55$, $p < .0001$; alpha$_1$: $F(2, 32) = 23.45$, $p < .001$; beta$_1$: $F(2, 32) = 7.86$, $p < .005$; beta$_2$: $F(2, 32) = 4.83$, $p < .05$; Fast: $F(2, 32) = 3.99$, $p < .05$;] except for alpha$_2$ [$F(2, 32) = 3.91$, $p < .06$].
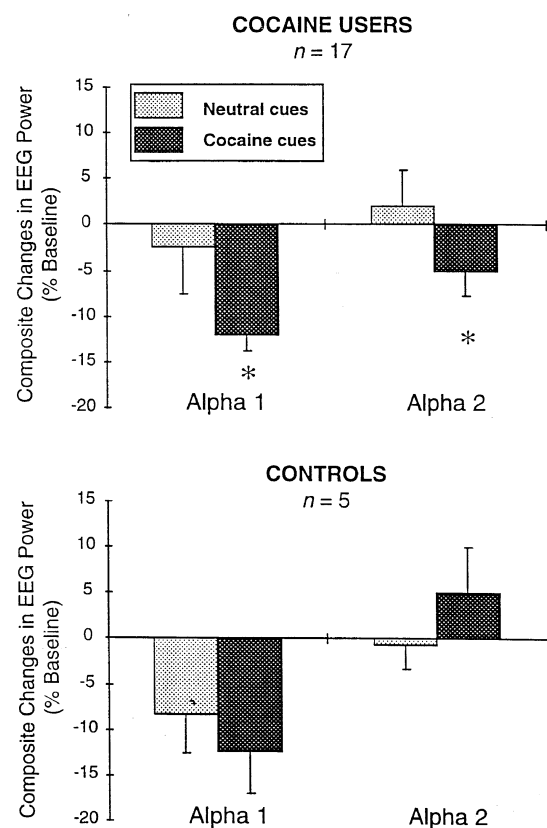

Figure 1. Reductions in EEG alpha power are greater following exposure to cocaine cues than after neutral cues in cocaine users. Composite changes in EEG each represent the mean percentage of change in power from baseline of all six leads over the three cue-presentation sessions. Error bars represent the SEM. An * indicates a significant difference at $p < .05$ determined by a repeated measures ANOVA of the cocaine user data. A separate ANOVA indicated no significant changes in alpha power within the control group.
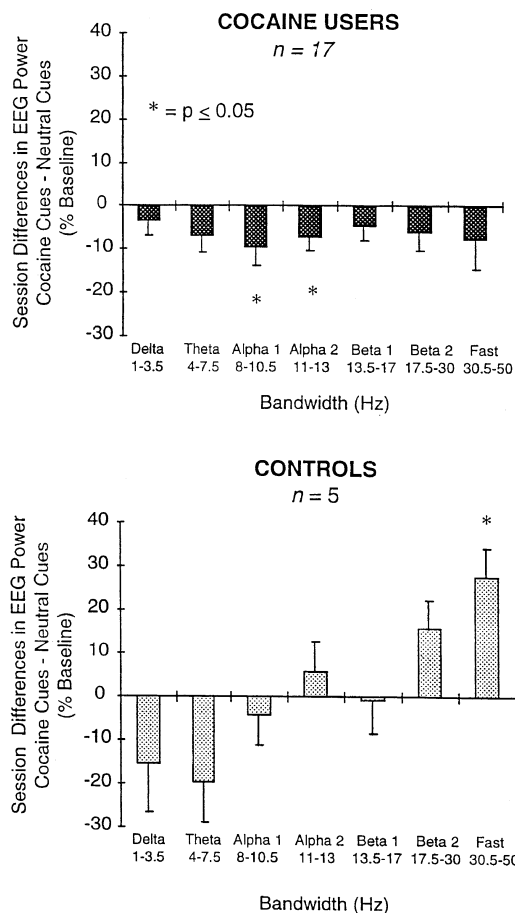
Figure 2. Exposure to cocaine and neutral cues differentially affects EEG power distribution in cocaine users and controls. For each subject group, differences (± SEM) in composite power between the cocaine cues and neutral cues presentation sessions are plotted for each bandwidth, with composite values representing an average over all six leads and the three cue-presentation trials within an experimental session. An * indicates a difference at $p < .05$ as determined by separate, repeated measures ANOVAs for the cocaine users and controls.
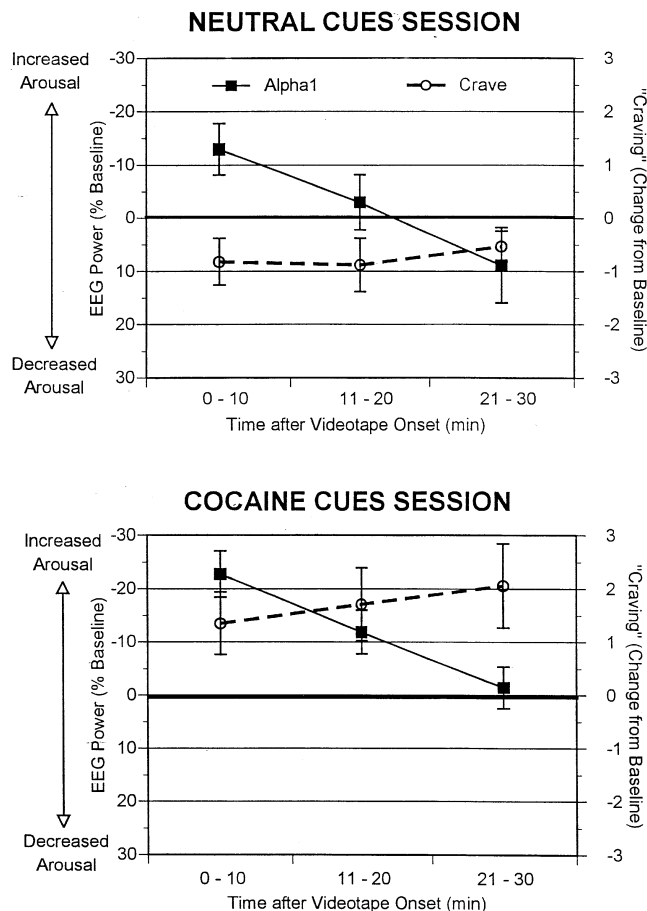
Figure 3. Differing patterns for time-dependent changes in EEG arousal and cocaine craving are displayed for the neutral cues (*upper panel*) and cocaine cues (*lower panel*) sessions in cocaine users. The left ordinates present changes in EEG power, expressed as percentages of baseline values; to better illustrate the reductions in EEG power, the left ordinate scales are reversed. Changes in alpha$_1$ power, a measure of arousal, are presented. The right ordinates indicate the change in craving score in each of the three videotape cue presentation periods relative to the prevideotape baseline period. Each point is the mean (± SEM) of 17 observations.

The pattern of time-related changes consisted of an initial reduction in power within the first EEG acquisition period, with subsequent increases throughout second and third acquisition periods, as shown in Figure 3 for the alpha$_1$ bandwidth. A leads main effect, reflecting variation in EEG power as a function of the recording site, was found in the two alpha bands [alpha$_1$: $F(5,80) = 3.72$, $p < .05$; alpha$_2$: $F(5,80) = 3.67$, $p < .05$]. A significant interaction between recording sites and recording periods (leads × time) was found for the alpha$_1$ [$F(10,160) = 2.67$, $p < .05$], beta$_1$ [$F(10,160) = 3.84$, $p < .01$], beta$_2$ [$F(10,160) = 3.24$, $p < .05$] and theta [$F(10,160) = 3.04$, $p < .05$] bands. In the theta band, a significant leads × session interaction [$F(5,80) = 2.97$, $p < .05$] was also present. No other interactions were demonstrated.

Within the control group, the only significant Session effect observed was for the fast activity band [$F(1,4) = 19.92$, $p < .05$] (Figure 2). This difference represented an increase in fast activity power relative to baseline across all leads during the cocaine cues presentation as compared with little or no change in power during the neutral cues presentation. The significant increase in power between sessions for fast activity as well as the differences in the other EEG bands in the control group are presented in Figure 2. A significant time effect occurred only for alpha$_1$ power [$F(2,8) = 10.89$, $p < .05$] and represented a trend for power to increase throughout the three 10-min periods during both test conditions in the control subjects similar to the pattern observed in the cocaine users (Figure 3).

Self-Reports of Cocaine Craving

The cocaine-using group reported greater desire for cocaine during the cocaine cues session than during the neutral cues session, as indicated by a significant main effect of session (cocaine vs. neutral) for the items "Do you have a craving or urge for cocaine?" [$F(1, 16) = 14.74, p < .001$] and "Do you want cocaine?" [$F(1, 16) = 7.24, p < .05$]. The session main effects for the remaining items: "How good do you feel?" [$F(1, 16) = 3.97, p < .07$]; "Do you need cocaine?" [$F(1, 16) = 4.07, p < .07$]; and "Are you turned off?" [$F(1, 16) = 3.55, p < .08$] did not reach the criterion for significance. The self-reports did not change across the three time periods in each session, as indicated by the lack of significant time effects or session × time interactions for all of the self-report questions, even though there was a trend in the scores for craving to increase during the cocaine cues session (Figure 3). The cocaine-naïve control group consistently reported scores of "0" in response to the five questions related to cocaine craving (data not presented).

EEG Arousal and Cocaine Craving Display Different Time-Dependent Changes

Because alpha$_1$ was the only bandwidth exhibiting both a significant difference between sessions and a significant main effect of time, it was examined for its relationship with self-reports of cocaine craving. As there were no session × leads or session × leads × time interactions in the ANOVA for alpha$_1$ power, changes in power were averaged over all six leads for this bandwidth for each 10-min block of time and the effects tested for correlation with self-report data. Figure 3 illustrates different patterns for the time courses of cue-elicited cocaine craving in cocaine users and of changes in EEG power. Furthermore, changes in self-reported craving for cocaine were not correlated with the changes in EEG power at any of the individual time points or when the data were collapsed across the entire session. The largest correlation occurred within the third 10-min epoch (30-min after the onset of the cues) between the changes in alpha$_1$ power and craving scores ($r = -0.44, n = 17, p < .08$).

Relationship between EEG and CMRglc

In contrast to the lack of correlation between EEG signs of arousal and self-reports of cocaine craving, the decreases in EEG spectral power did show significant correlations with increases in CMRglc. Analysis of correlations between session differences in EEG power and differences in CMRglc were restricted to the alpha$_1$ and alpha$_2$ frequencies, the only bands to be differentially affected by the cocaine cues and neutral cues in cocaine

users. Because CMRglc reflects brain metabolism integrated over a 30-min period (McCulloch 1982), CMRglc was compared to EEG data from the first 10-min period as well as the EEG data collapsed across the 30-min session.

The overall decrease in alpha$_1$ power between the cocaine and neutral sessions was correlated with the corresponding net increases in global brain glucose metabolism. Figure 4 illustrates the significant correlation between the difference in alpha$_1$ power during the first 10 min of the cues presentation and CMRglc determined over 30 min ($r = -0.74, n = 8, p < .03$). When changes in alpha$_1$ power were integrated over 30 min, represented by summing the three values obtained during entire cue presentation period, the correlation of session differences with net differences in CMRglc was only slightly larger ($r = -0.78, n = 8, p < .02$) (data not presented). A similar, but less robust relationship was present between reduced alpha$_2$ power over 30 min and increased CMRglc ($r = -0.68, n = 8, p < .06$) (data not shown). There was no correlation of the 10-min alpha$_2$ differences and CMRglc ($r = 0.42, n = 8, p < .30$). These relationships suggest that EEG signs of arousal, as indexed by decreased power (desynchronization) in the alpha bands, are associated with increased brain metabolism.
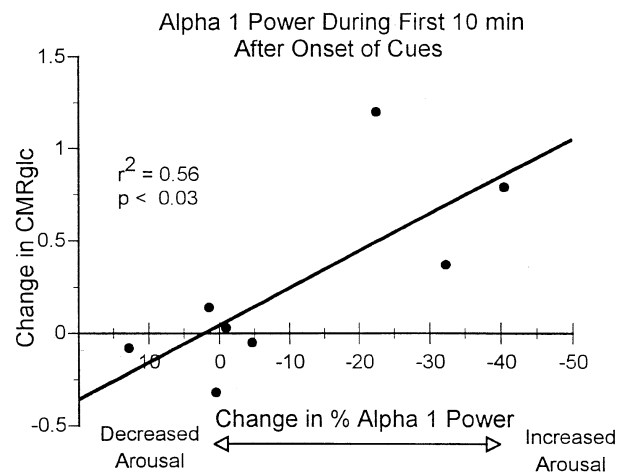

Figure 4. Relationship between EEG arousal (decreases in alpha$_1$ power) developing within the first 10 min after cue presentation and CMRglc in the eight subjects who had both complete EEG and PET data sets. Note that values on the abscissae are plotted with negative values on the right rather than the left (i.e., in reversed order) to emphasize the positive relation between increases in EEG arousal (decreased alpha$_1$ power) and increases in CMRglc. The change in alpha$_1$ power between the first 10-min periods of the two cue sessions is expressed as the percent change from the baseline period in the cocaine cues session minus the percent change in neutral cues session. On the ordinate, cocaine cues minus neutral cues session changes in CMRglc are expressed as mg/100 g/min.

DISCUSSION

Results from this study can be summarized as five broad findings. First, controls and cocaine users exhibited different patterns of EEG changes to cocaine-related cues. Second, presentation of cocaine-related cues to current users of cocaine produced an increase in EEG arousal (desynchronization), evidenced most clearly by the sharp decline in EEG power in the alpha$_1$ bandwidth when the stimulus-complex was presented. Third, the EEG arousal was transient, in that there was a gradual increase in EEG power (increased synchronization) over the 30-min session despite the continuing presence of the cocaine-related stimulus complex. By the end of the stimulus presentation period, EEG arousal had returned to prestimulus baseline levels. Fourth, EEG arousal was diffuse in terms of both topography and bandwidth, that is to say similar changes in EEG arousal were seen at all of the electrode sites and frequency ranges. Finally, EEG arousal was not related to the individual differences in self-reports for cocaine craving, indicating that cocaine craving is not a simple reflection of a generalized arousal state. Nevertheless, EEG arousal was correlated with CMRglc, suggesting that both of these measures index generalized cortical activation.

Although we used a different study design and a more limited sample of electrode sites, the present findings are consistent with earlier reports (Bauer and Kranzler 1994; Hersh et al. 1995) that exposing subjects with a history of cocaine dependence to films featuring cocaine or erotic stimuli generally diminished EEG power and increased self-rated desire for cocaine as compared with responses to a neutral stimulus. Unlike the previous studies where EEG measurements during cue exposure were restricted to a single 5-min period, we monitored EEG changes across an expanded time period and demonstrated that after an initial reduction in EEG power, cocaine using subjects habituated to the stimuli during both the neutral cues and cocaine cues sessions, as indicated by the gain in EEG power over time (Figure 3). Nonetheless, during each time period, subjects who used cocaine consistently manifested lower EEG power throughout the cocaine cues session than during the neutral cue session. Thus, even with prolonged exposure to similar stimuli, cocaine abusers are more aroused than when they are exposed to neutral stimuli.

Exposure to cocaine cues produced a greater desire for cocaine in our cocaine-experienced subjects than did the neutral cues as reported previously (Bauer and Kranzler 1994). It is noteworthy that as the initially reduced EEG power increased over the course of the three cue exposure periods (a decrease in activation), self-reports of cocaine craving as well as wanting cocaine remained statistically stable throughout the experiment. A lack of correlation between decreased EEG power and craving was also reported previously by Bauer and Kranzler (1994), and the present study extends this prior finding to delineate a separation over time between these two entities. As shown in Figure 3, alpha$_1$ power, which is reduced within the first 10 min of exposure to the cocaine cue videotape, returns toward baseline during the next 20 min. In contrast, craving and wanting (data not presented) responses over 30 min plateaued or tended to increase slightly above baseline levels. If one accepts the assumption that a diffuse pattern of decreased EEG power reflects general arousal, then craving can be viewed as sharing characteristics with, but not being dependent on, a general state of arousal. This explanation is supported by the absence of a correlation of decreased EEG power with self-reported craving states and the tendency for diminished EEG power to be negatively correlated with increased CMRglc.

The pattern of responses of the present control group was different from those of the cocaine user group in the present study and those of the control subjects in a previous study (Bauer and Kranzler 1994). In the present study, control subjects exhibited a significant increase in power in the fast activity band during exposure to cocaine-related stimuli, as contrasted with the decreases in power in the slower spectral bands in the cocaine-using subjects. Although Bauer and Kranzler (1994) did not measure EEG power above 27.6 Hz, the increase in fast activity in our control subjects also stands in contrast to the uniform decreases in power across all of the EEG spectral bands observed in response to cocaine-related stimuli in both cocaine-using and control subjects in the report by Bauer and Kranzler (1994). Despite the differences in the EEG patterns, however, cocaine-related stimuli did not elicit reports of cocaine craving in the control subjects in either the present study or the prior study (Bauer and Kranzler 1994). This apparent discrepancy between the EEG activity in the control groups across the two studies, should, however, be viewed with caution because of the relatively small sample size of the control group and the resultant lack of statistical power in the present study.

In conclusion, the diffuse topography of the EEG desynchronization appears to reflect a general brain state (i.e., cortical arousal) elicited during the cocaine cues condition as indicated by the correlation of the EEG changes with whole brain glucose metabolism (CMRglc). In contrast, the neural substrates of craving may be more localized in discrete brain regions as suggested by our previously reported correlations of craving with regional glucose metabolism in dorsolateral prefrontal cortex, amygdala, and cerebellum (Grant et al. 1996). Changes in the neural activity of these structures may not be reflected efficiently in changes in the EEG at specific scalp recording sites. Although the general reduction of EEG power may provide a brain state that con-

tributes to cognitive processes leading to self-reports of craving, the present results indicate that once these processes are initiated, craving becomes dissociated from the background arousal state and follows its own course.

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